SMMGP CLINICAL UPDATE

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The SUMMIT trial: a field comparison of buprenorphine versus methadone maintenance treatment.

Pinto H, Maskrey V, Swift L, Rumball D, Wagle A, Holland R. J Subst Abuse Treat 2010;39:340-352

This study took 361 opiate-dependent individuals who presented for treatment over 2 years at a drug service in England. They were spread over three sites within one community drug team in Norfolk.

They received rapid titration then flexible dosing with either methadone or buprenorphine. After consultation and discussion it was left to the patients to decide what they wanted: 227 chose methadone (63%) and 134 buprenorphine (37%). Those who opted for methadone had more severe substance abuse, psychiatric and physical problems.

The results showed that despite the more severe nature of the problems in the methadone group they were more likely to be retained in treatment. The survival analysis suggested they were over twice as likely to be retained. However, the buprenorphine group were twice as likely to suppress illicit opiate use and to achieve detoxification. The authors also noted that buprenorphine may improve recruitment into treatment as 28% of those who opted for it stated they would not have gone into treatment to have taken methadone.

Other results also showed predictors of retention: the strongest factor was treatment choice but other factors included older age, fewer custodial sentences and non drug-using parents.

SMMGP comment:
The authors declare that this 'is the first large study to compare the effectiveness of buprenorphine maintenance with methadone maintenance in ordinary UK clinical practice'. The problem with RCTs, as necessary as they are, is that it can always be argued that they don't represent true clinical practice and so this was a prospective patient preference study. There was no randomisation and the individuals chose which treatment they wanted.

One of the criticisms of buprenorphine RCTs has been that the inductions weren't fast enough. This study is more aligned with true practice (at least in terms of the buprenorphine inductions) but it is worth highlighting that the methadone inductions generally exceeded the 2007 Clinical Guideline recommendations with mean doses on day 1 of 50.7mg (0-135mg), day 2 of 63.8mg (5-160mg) and day 3 of 69.6mg (5-170mg). There were two deaths in the study – both from the methadone group and one of them was related to methadone toxicity.

Careful interpretation of pragmatic studies like this can add to our knowledge and the results will not come as a massive surprise to anyone involved in opiate substitution therapy. These results add credibility to what would otherwise remain anecdotal evidence.

Neonatal abstinence syndrome after methadone or buprenorphine exposure.

Jones HE, Kaltenbach K, Heil SH, et al. N Engl J Med 2010;363:2320-31

One has to commend the authors for the succinct title of this paper as what this study was really doing was comparing methadone versus buprenorphine in a double-blind, double-dummy, flexible-dosing, randomised controlled study.

They recruited 175 pregnant women with opioid dependency at 8 international sites. They were randomised to methadone or buprenorphine. The primary outcomes were the number of neonates requiring treatment for neonatal abstinence syndrome (NAS), the peak NAS score, the total amount of morphine needed to treat NAS, the length of hospital stay for the neonates and neonatal head circumference.

The results showed that treatment was discontinued by 16 out of 89 women who had methadone (18%) and 28 of the 86 women in the buprenorphine group (33%). The results

looked at those who were followed to the end of pregnancy. In these women the infants in the buprenorphine group required significantly less morphine (mean dose 1.1mg vs 10.4mg; p<0.009) and had a shorter duration of treatment for NAS (4.1 days vs 9.9 days; p<0.003). There were no other significant differences and no difference in rates of maternal or neonatal adverse events.

There was no difference in the maternal rates of opioid use during treatment.

tempered with the higher drop out rate. Some might argue that the drop out rate has boosted the relative benefits of buprenorphine but the authors have also done some post-hoc analysis and the differences remain significant.

The authors rightly highlight that it would now be reasonable to consider buprenorphine as first-line treatment for opioid dependence in pregnancy. The challenge for clinicians faced with these women is to identify those that will stick with it and to reduce that drop-out rate.

Methadone dose and neonatal abstinence syndrome – systematic review and meta-analysis. *Cleary BJ, Donnelly J, Strawbridge J, et al. Addiction 2010;105:2071-2084*

A total of 67 studies met the inclusion criteria and 29 were included in the meta-analysis. Any differences in the incidence of NAS in infants of women on higher compared with lower doses were statistically insignificant in analyses restricted to prospective studies or those using an objective scoring system.

SMMGP comment:
The systematic review of methadone dose and NAS can be summed up easily – they don't seem to be linked. So, for those women on methadone in pregnancy we should treat the mother with the dose she needs and not with fear of worsening NAS.

The NEJM study is methodologically impressive. The lack of difference between groups in terms of opioid use in that study isn't unexpected – we know that treatment outcomes are similar for methadone and buprenorphine. Equally, we also know that methadone retains better and, as discussed above, in the SUMMIT trial all the data point towards this difficulty buprenorphine has in retaining people in treatment compared with methadone.

However, in terms of neonatal outcomes buprenorphine trumps methadone in 2 out of 5 primary outcomes but obviously this has to be

Women who inject drugs: A review of their risks, experiences and needs. A report prepared on behalf of the Reference Group to the United Nations on HIV and Injecting Drug Use. *National Drug and Alcohol Research Centre (NDARC), University of South Wales, Australia, 2010.*

This is a huge report summarising the issues for women who inject drugs. It is a systematic review of the literature but also includes non-peer reviewed ('grey') literature and expert consultation.

The report highlights that women who inject have substantially different needs and face higher risks of disease and violence than men who inject drugs. The majority of IDUs are men but the women have significantly higher mortality rates, faster progression from first use to dependence, higher rates of HIV and increased risky injection and sexual risk behaviours.

Novice female injectors have higher seroprevalence rates for HIV than male injectors with the same duration of injection use. There are several factors which can act as predictors of those who will start injecting and these are: involvement in sex work, non-injecting drug use, lifetime history of sexual abuse, exposure to trauma and violence, social network that includes IDUs, family history of drug use, homelessness or low socio-economic status, lifetime history of incarceration, young age at first illicit drug use, same sex attracted

women, early sexual experiences, mental illness and suicide attempts.

Women are more likely to inject in a social setting and are more likely to be injected by someone else, often male. The report noted that, perhaps counter-intuitively, women who have sex with women (WSW) are at higher risk of HIV than heterosexual women.

Sex work is a major independent risk factor for HIV in female IDUs. As well as sex work some female IDUs report transactional sex relationships where the intimacy with the partner is tied to shelter, food, drugs and/or protection. These women may be vulnerable as they may be less capable of insisting on safe sex or injecting behaviours. Intimate partner violence (IPV) is three times more likely in IDU partnerships.

SMMGP comment:
The essential theme in this report is that women who inject drugs have different needs to men. The suggestion is that those needs are under-represented in the literature. We would also suggest those needs are probably not being fully considered in practice. We know that white women and even more so women of colour and lesbians are
under-represented in UK drug treatment.

Experience shows this is multi-factorial and includes male dominated environment, inconvenient opening hours, lack of child care facilities and fear of social services.

Treatment services need to be tailored to encourage women into treatment. There is little evidence around best treatment for women but the report emphasises the importance of pregnancy services, child care facilities and low threshold services for women. Service provision can be slow to change but we can, at least, tailor our personal clinical practice to their needs.

Primary care-based intervention to reduce at-risk drinking in older adults: a randomized controlled trial. *Moore AA, Blow FC, Hoffing M, et al. Addiction 2010;106:111-120*

This study in California took 631 at-risk drinkers aged over 55 and randomly assigned them to two different groups. The control group received 'usual care'; which in this case consisted of a visit to the clinic to receive a booklet on healthy behaviours. The intervention group had a

personalised report, a booklet on alcohol and ageing, drinking diary, advice from the primary care provider and telephone counselling from a health educator at 2, 4 and 8 weeks.

The primary outcome was the proportion of participants who met the at-risk criteria - assessed using the Comorbidity Alcohol Risk Evaluation Tool (CARET). They also looked at secondary outcomes such as the number of drinks in the past 7 days and heavy drinking (4+ drinks per day) in the past 7 days.

The results showed that at 3 months there were fewer intervention group members who were at-risk drinkers (OR 0.41); they reported drinking fewer drinks in the past 7 days and had lower risk scores. At 12 months the only outcome that remained significant was that the intervention group reported drinking fewer drinks.

SMMGP comment:
This paper was considering at-risk drinkers and the point was that older drinkers have even greater risks associated with alcohol – hence the use of the CARET tool that considers relevant factors such as other medications and comorbidities. Using this definition they reported that 18% of men and 5% of women over 60 in the US were at-risk. It has been shown that these people have a 20% higher mortality than not at-risk drinkers – it makes sense to target this group.

There was a fairly hefty intervention in this study – as the authors stated it was certainly 'multi-faceted'. Yet, it still made little difference

to long-term outcomes. It would be difficult to justify providing this level of intervention to nearly 1 in 5 of the population with marginal improvements. Perhaps the studied group is too diverse; we have simply cast the net too wide and an even more targeted approach is needed.

However, on a more positive note it is worth pointing out that in both groups, intervention and control, the prevalence of at-risk drinking dropped by 50-60% from baseline to 3 months and was still largely there at 12 months. It may be that the simplest of interventions is as helpful - but it may also be that older drinkers tend toward less risky alcohol habits as they age regardless of our efforts to influence their drinking.

Outpatient versus inpatient opioid detoxification: a randomized controlled trial. *Day E, Strang J. J Subst Abuse Treat 2011;40:56-66*

This study took 68 opioid-dependent patients who were in community treatment who were requesting detoxification. They were then randomly assigned to either an inpatient or an outpatient setting for their detoxification. Three-quarters (78%) of those in community treatment wanting detoxification were taking methadone at a mean dose of 33mg but only 51% had been taking it every day in the month preceding detoxification.

The results showed that more inpatients (n=18, 51.4%) than outpatients completed their detoxification (n=12, 36.4%) but this was *not* statistically significant. However, the outpatient group received a longer period of medication and when this was controlled for the results did favour the inpatient setting.

The longer term results should be noted: only 11 patients of the initial 68 were opioid free at the 1-month follow-up and only 8 patients at the 6 month follow-up.

SMMGP comment:
It shouldn't come as a huge surprise that in-patient detoxification is more successful in terms of completion but it is the long-term outcomes that matter. The long-term results ram the issue down our throats. Only 8 patients (11.7%) were opioid free at the 6 month point. Buried in the results section are the comments on post-detoxification care which showed that only 2 (out of a total of 30) detoxification completers had access to a residential rehabilitation program (this was in 2001-3). Only 1 participant attended a local abstinence-based day program, but this service closed 6 months after the start of the trial. So, overall the access to post-detoxification care was pitifully low.

The authors state "opioid detoxification is not an effective stand-alone treatment for heroin dependence but is nevertheless an essential step in the path to recovery". This study demonstrates and confirms that statement. We will create further barriers if new policy vilifies opiate substitution therapy and compromises its provision.

We should be under no illusions that we have a mountain to climb to convert short-term detoxification outcomes into long-term abstinence and recovery. Although this study relates to 2003 it feels as if the access to rehab has worsened since then. We must strive to not only increase this access but also to ensure that commissioners do not insist on mandatory percentages to enter detoxification without robust after care - or deaths will rise.

Innocent parties or devious drug users: the views of primary healthcare practitioners with respect to those who misuse prescriptions drugs. *Butler R, Sheridan J. Harm Reduct J 2010;7:21*

In this qualitative study in New Zealand interviews with general practitioners, community pharmacists and other 'key experts' were completed, transcribed and underwent thematic analysis. The researchers were interested in the

attitudes and experiences associated with prescription drug misuse.

One major theme identified was that the practitioners felt that prescription drug misuse patients fell into two different types. These were the 'abuser' and the 'overuser'. The abuser was thought to be using deception to get drugs for their own use or to sell; whereas the overusers were thought to have become 'addicted' through inadvertent overuse or over-prescription.

Naturally, the 'overuser' was viewed more sympathetically than the 'abuser'.

However, this also had a further impact with an effect on whether any harm reduction would be offered. Additionally, the authors noted that while there was more sympathy toward the 'overuser', there was a lack of appropriate services for this group and no peer group support network.

SMMGP comment:
This is a really useful qualitative paper that helps give clarity to some of the thoughts and beliefs many of us may have swirling around in regard to prescription drug misuse. It doesn't advocate or recommend
splitting people into different sub-groups – that finding has emerged from the data and reflects how practitioners perceive people. Indeed, the authors suggest that this "binary view may not be helpful".

Nowhere is it clearer than with something like benzos – our drug services are not well configured to deal with prescription drug misusers and we are stigmatising another group. Clearly, we need to have a good awareness of our own personal judgements and preconceived ideas but it also points toward a wider educational need for clinicians. See RSA report mentioned in policy update and interesting article in next Network on stigma – the most important obstacle left to overcome to improve lives for people who use drugs.

The prevalence and correlates of buprenorphine inhalation amongst opioid substitution treatment (OST) clients in Australia. *Horyniak D, Dietze P, Larance B, Winstock A, Degenhardt L. Int J Drug Policy 2010, doi:10.1016/j.drugpo.2010.10.004*

This short report looked further at the issue of buprenorphine diversion. They had a cross-sectional sample of 440 clients on opioid substitution treatment. They were recruited through pharmacies and clinics and interviewed face-to-face with a structured questionnaire. They excluded those who had never used buprenorphine.

The results showed that 65 people (18%) reported ever having inhaled buprenorphine. Logistic regression showed that those who were significantly more likely to have inhaled had the following characteristics: aged 35 or younger, been in prison, and a history of having ever injected buprenorphine.

SMMGP comment:
This is one of the very first studies to comment on the snorting and inhalation of buprenorphine. However, it is notable that their definition of inhalation also included smoking of buprenorphine and very few were actually nasal snorting – only 6% of buprenorphine inhalers.

Anecdotally, anyone working in this area in the UK will be aware of the high use of buprenorphine and buprenorphine-naloxone snorting and particularly its widespread use across the prison estate.

The smoking of these drugs is not obviously an issue in the UK but this study does serve to remind us that people will always finds new and imaginative ways to use and abuse mind-altering substances.

Pulmonary function in cannabis users: Support for a clinical trial of the vaporizer. *Van Dam NT, Earleywine M. Int J Drug Policy 2010;21:511-513*

This short report looks at the use of a cannabis vaporiser; this is a small device that heats the cannabis to release cannibinoids in a mist without smoke and other irritants.

They took 22 frequent cannabis users who weren't interested in stopping their use. They had to have reported at least two respiratory symptoms and they then completed subjective ratings of respiratory symptoms and spirometry pre and post 1 month's use of a vaporiser.

The outcomes were the self-reported severity of nine respiratory symptoms and spirometry – including FEV1 (forced expiratory volume in 1 second) and FVC (forced volume vital capacity). In the results 2 failed to follow up and 4 participants reported smoking cannabis and so were excluded. The results showed that they had significantly improved respiratory symptoms and FVC. FEV1 improved but not significantly.

SMMGP comment:
If you want to take a look at the vaporiser then visit YouTube (tinyurl.com/vaporiser) to see a similar model from the same company as the one given to the participants in the trial.

This study highlights one of the biggest harms associated with regular cannabis use. The respiratory damage caused by cannabis has been well documented and is largely attributable to smoking unfiltered tobacco.

Cannabis smokers probably take deeper drags, hold the smoke in their lungs for longer and have a tendency to smoke right down to the roach. All of these are likely to add to the harms of using tobacco.

There was a history of tobacco use in 24% of the starting sample. If we assume that most people were smoking cannabis with tobacco then effectively the vaporiser has removed tobacco use from three-quarters of the sample.

The authors also comment that the changes are in line with those seen after cessation of long-term tobacco use.

The authors report that the vaporiser has potential as a device for the administration of medical cannabis and also as a harm reduction technique. We'd be wary of the interpretation of the self-reported measures – clearly there was no blinding and the subjective bias will be massive. However, the spirometry results are compelling and warrant further assessment.